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Psychosocial Functioning after Discontinuation of Long-Term Growth Hormone Treatment in Girls with Turner Syndrome

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Key Words

Growth hormone therapy · GH trials, psychological evaluation · Turner syndrome · Turner syndrome, final height · Turner syndrome, short stature

Abstract

It is common practice in the case of Turner syndrome (TS) to treat short stature with GH treatment and to induce puberty with estrogens at an age as close to normal puberty as possible. This approach in most cases leads to a height in the normal range in childhood, adolescence, and adulthood in TS. Little data is available, however, on its effect on psychosocial functioning. In the present study, we evaluated psychosocial functioning in a group of 50 women with TS, after reaching final height in two multicenter GH trials. Thirty-six girls participated in a randomized dose-response study from mean (SEM) age 6.8 (0.4) years, and 14 girls participated in a frequency-response study from age 13.2 (0.4) years. After discontinuation of long-term GH treatment, these 50 girls were evaluated for psychosocial functioning at a mean age of 18.8 (0.3) years. GH was given in a dosage of 4 IU/m²/day (~0.045 mg/kg/day), 6 IU/m²/day, or 8 IU/m²/day. After a mean GH treatment duration of 7.1 (0.4) years, mean final height (ref. normal girls) was FH1.2 (0.2) SD score. Behavioral problem scores (Achenbach) of the TS women were comparable to normal Dutch peers. Although self-per-

ception (Harter total scale: $p < 0.01$), and bodily attitude (Baardman: $p < 0.05$) was significantly less positive than for their normal Dutch peers, we found no evidence of depression. TS women rated their family functioning higher than their Dutch peers ($p < 0.0001$), and had a slightly different coping pattern. These results show that even after reaching a height in most cases within the normal range and puberty induction at a pubertal age, some women with TS still experience psychosocial problems. It is likely, however, that GH and estrogen treatment improved psychosocial functioning. Long-term follow-up of these GH-treated patients will allow an evaluation of their life achievements.

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Introduction

The most frequent clinical characteristics of Turner syndrome (TS) are short stature and the absence of spontaneous pubertal development. In most countries it is common practice to treat short stature in TS with GH treatment in a supraphysiological dosage. In addition, estrogens are given to induce puberty at an age as close to normal puberty as possible. This approach has been shown to increase and even normalize height in childhood, adolescence, and adulthood in TS [1–5]. Little data is available, however, on the effect of this treatment strat-

egy on psychosocial functioning. Untreated girls with TS have been described as being more immature, having a lower self-esteem, poor concentration, and being hyperactive [6, 7].

In the present study, we evaluated psychosocial functioning in a group of 50 women with TS, after reaching final height in two multicenter GH trials.

Methods

GH Group

All women who had participated in two GH trials (see below), had discontinued GH treatment for more than 6 months, and were able to fill in the questionnaires, were asked to participate in the psychosocial evaluation. Fifty women agreed to participate (response rate 50/69: 72%). Nineteen girls did not participate either because of practical reasons or because of losing interest in participating in a study.

Both GH trials evaluated the effect of GH on long-term growth and ultimately on final height (FH). At time of the psychosocial evaluation, all participants were prescribed hormone replacement therapy in an adult dose.

Dose-Response GH Trial

Sixty-eight previously untreated Dutch girls with TS, aged between 2 and 11 years, were enrolled in an open randomized multicenter GH dose-response study (DRS). Biosynthetic GH (r-hGH Norditropin®, Novo Nordisk A/S, Denmark) was given subcutaneously once daily in a dosage of 4, 6, or 8 IU GH/m² body surface area/day (~0.045–0.09 mg/kg/day). Puberty was induced at age 12 years (study design as described previously [5]). Six girls dropped out of the study and were lost to follow-up. Six girls had not discontinued GH treatment for more than 6 months and 4 girls were unable to fill in the questionnaires due to mental retardation, leaving 52 girls able to participate in the psychosocial evaluation.

Frequency-Response GH Trial

Nineteen previously untreated Dutch girls aged 11 years or older, with TS, were enrolled in an open randomized multicenter GH frequency-response study (FRS). Biosynthetic GH was given subcutaneously once or twice daily in a total dosage of 6 IU GH/m²/day. Puberty was induced at start of trial (study design as described previously [1]). Two girls were unable to fill in the questionnaires due to mental retardation, leaving 17 girls able to participate in the psychosocial evaluation.

The GH trials and the psychological evaluation were approved by the Ethics Committees of the participating centers in the Netherlands. Written informed consent was obtained from the parents or custodians of each child.

Normal Population Sample

From a randomly selected population sample from three municipalities in the Netherlands (n = 600, response rate 56%), only the females were selected for comparison (n = 359) [8].

Psychosocial Evaluation

In the GH group a psychosocial evaluation was performed after GH treatment had been discontinued for at least 6 months and

(near) FH had been reached. Questionnaires for the GH trial groups and the population sample were sent by post.

General Information. Data on occupational and educational levels were provided by both parents and adolescents. Parental occupational level (SES) ranged from 1 (lower occupation) to 3 (higher occupation). When both parents were employed the highest of both SES levels was used. For unemployment the lowest SES was used [9].

Behavioral Problems (YSR/YASR). Behavioral problems were measured by 3-point scale standardized questionnaires from Achenbach, translated and validated in the Dutch language [8, 10, 11]. For girls aged between 12 and 18 years, the 119-item Youth Self-Report (YSR; filled in by child) [12, 13] was used. For girls aged 18 years and older, the 127-item Young Adult Self-Report (YASR; filled in by adolescent) was used [14]. As both questionnaires were constructed in a similar way, results from three scales could be combined for analysis (Internalizing, Externalizing, and Total Problem score). To allow combination of test scales (YSR/YASR), z-scores were constructed using the Population sample data as reference [8]. A higher test z-score indicated more problem behavior.

Self-Perception (HSPP). The inventory, called in Dutch 'Hoe ben ik' and in English 'Harter Self Perception Profile', was designed by Harter to describe sense of self-worth and capability in several areas, using 4-point scales. [15, 16]. In the evaluation the 45-item adolescent-version (HSPP-a) was used. Ten scales (Scholastic competence, Social acceptance, Athletic competence, Physical appearance, Behavioral conduct, Global self-worth, Romantic appeal, Close friendship, Job competence, and Total HSP score) were used for analysis (median $\alpha = 0.76$). A higher test score indicated a more favorable self-perception.

Child Depression Inventory (CDI). The American Child Depression Inventory was designed to measure depressive thoughts and feelings in a child population and was designed by Kovacs [17]. Factor analysis of the Dutch version of the 27-item (3-point scales) 'Gevoelens en Gedachten vragenlijst' produced one scale, the 'Total depression scale score' ($\alpha = 0.86$) [8]. A higher score indicated more depressive thoughts and feelings.

Body Attitude Scale (BAS). The Dutch questionnaire 'Lichaamsbelevings vragenlijst' is a 45-item questionnaire and uses a 5-point Likert scale to assess bodily attitude. It has been constructed and validated by Baardman et al. [18]. In an adolescent population, three scales could be distinguished by factor analysis: 'Appraisal' ($\alpha = 0.94$; e.g. 'Are you satisfied with the way your body looks?'), 'Attribution' ($\alpha = 0.88$; e.g. 'Do you think people avoid you because of your appearance?'), and 'Physical contact' ($\alpha = 0.77$; e.g. 'In general, how much do you like touching people?') [8]. High test scores indicated positive bodily attitudes.

Family Assessment Device (FAD). This shorter 12-item version of the General Functioning Subscale of the McMaster Family Assessment Device measured overall family functioning, using a 4-point scale. Reliability and validity were tested in the original language [19] and in Dutch [20]. A higher test score indicated more positive family functioning.

Coping (UCL). The 'Utrecht Coping list' [21] was designed and validated in Dutch [22, 23]. The 47-item 4-point scale list was made to measure 7 ways of coping with stressful events: Active approach (e.g. 'In general, if I have a problem I tackle the problem immediately'), Reassuring thoughts (e.g. 'In general, if I have a problem I encourage myself'), Expression of emotion (e.g. 'In general, if I have

Table 1. Mean (SEM) clinical data for the girls who participated in the psychosocial evaluation and for the Population sample

	Dose-response group (GH 4–8 IU/m ² /day)	Frequency-response group (GH 6 IU/m ² /day)	Population sample
Number of girls	36	14	359
Chronological age at start GH trial, years	6.8 (0.4) ^{##}	13.2 (0.4)	–
Height SD score at start (ref. normal Dutch girls)	–2.7 (0.2)	–3.2 (0.3)	–
Final height SD score (ref. normal Dutch girls)	–1.0 (0.2) [#]	–1.9 (0.2)	–
Target height SD score	–0.2 (0.2)	–0.3 (0.2)	–
Age start puberty (B2), years	12.7 (0.1)	13.2 (0.4)	–
GH duration, years	8.5 (0.3) ^{##}	3.6 (0.2)	–
Karyotype: 45,X	30 (83%)	10 (71%)	–
Karyotype: other	6 (17%)	4 (29%)	–
Age at psychosocial evaluation, years	18.2 (0.4) [#]	20.4 (0.4) ^{**}	17.1 (0.2)

GH = Growth hormone.

One-way ANOVA: ** $p < 0.001$; two-tailed (GH group vs. Population sample).

[#] $p < 0.01$, ^{##} $p < 0.001$; two-tailed (Dose-response trial vs. Frequency-response trial).

a problem I show I am annoyed'), Palliative reaction (e.g. 'In general, if I have a problem I seek distraction from it'), Passive reactional pattern (e.g. 'In general, if I have a problem I see dark clouds'), Seeking social support (e.g. 'In general, if I have a problem I share it with someone'), Avoiding/Anticipating (e.g. 'In general, if I have a problem I leave it the way it is') (median $\alpha = 0.69$). A higher test score indicated the coping style was more prominent.

Statistical Analysis

All data were expressed as mean (SEM) unless otherwise specified. Differences in SES between the Population sample and the GH group were analyzed by logistic regression analyses. To analyze differences in results between the GH group and the Population sample regression analyses were used, corrected for age, GH trial (1 dummy variable: FRS = 1) and GH dosage (2 dummy variables). SES (2 dummy variables) was only corrected for when significant. The effect FH, corrected FH, and the increase in height from start of GH treatment were estimated by the addition of FH SD score, corrected FH SD score and height SD score at start to the regression models, with correction for age, GH trial, and GH dosage. Results from the regression analyses were shown as unstandardized coefficients (B) with their two-tailed p values. All calculations were done by SPSS 9.0. A p value of 0.05 was considered significant for comparison between the GH group and the normal sample. A p value < 0.01 was considered significant for within GH group comparison because of multiple testing.

Results

Clinical data of the GH trials are shown in table 1 for all women who participated in the psychosocial evaluation. We found no significant differences in clinical data between TS women participating in this psychosocial

study and TS women who did not participate. Psychosocial data for the DRS and FRS were analyzed together (GH group). Correction for GH trial (FRS or DRS) and GH dosage did not have a significant influence on results.

Social Economic Status (SES)

In the GH group, 35% had a low SES level, 20% an intermediate level, and 46% a high level. The differences in SES between the GH group and the Population sample (33/34/33%, respectively) were not significant. Correction for SES did not significantly change any of the following results.

Behavior (YSR/YASR)

Internalizing, Externalizing, and Total problem behavior SD scores were comparable to the Population sample mean (table 2).

Self-Perception (HSPP)

Total HSP scores (table 3) were significantly lower than the Population sample scores ($B = -0.30$, $p < 0.01$), while GH dosage had no significant effect. To explain this result, we examined the remaining scale scores, which are the components of the Total HSP scores. Social acceptance, Athletic competence, and Romantic appeal scores were also significantly lower than the Population sample scores ($B = -0.63$, $p < 0.001$, $B = -0.55$, $p < 0.01$, $B = -0.40$, $p < 0.05$, respectively). The remaining scale scores were not significantly different to the Population sample scores.

Table 2. Mean (SEM) of the SD scores of the YSR/YASR questionnaires for self-reported behavioral problems

	GH group	Population sample
Internalizing SD score	0.3 (0.1)	0.0 (0.1)
Externalizing SD score	-0.1 (0.1)	0.0 (0.1)
Total problem behavior SD score	0.1 (0.1)	0.0 (0.1)

Regression analyses, corrected for age, GH trial, and GH dosage: No significant differences (GH group vs. Population sample).

Table 3. Mean (SEM) of the 10 scale scores of the Harter Self-perception profile

	GH group	Population sample
Scholastic competence	2.7 (0.1)	2.9 (0.0)
Social acceptance	2.5 (0.1)***	3.0 (0.0)
Athletic competence	1.9 (0.1)**	2.5 (0.0)
Physical appearance	2.3 (0.1)	2.6 (0.0)
Job competence	3.1 (0.1)	3.2 (0.0)
Romantic appeal	2.2 (0.1)*	2.5 (0.0)
Behavioral conduct	3.2 (0.1)	3.1 (0.0)
Close friendship	3.1 (0.1)	3.3 (0.0)
Global self-worth	2.8 (0.1)	3.0 (0.0)
Total HSP	2.6 (0.1)**	2.9 (0.0)

Regression analyses, corrected for age, GH trial, and GH dosage: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; two-tailed (GH group vs. Population sample).

Table 4. Mean (SEM) of the scores for the Child Depression Inventory (CDI), the Bodily Attitude Scale (BAS), and the Family Assessment Device (FAD)

	GH group	Population sample
CDI		
Total depression scale	1.3 (0.0)	1.3 (0.0)
BAS		
Appraisal	3.6 (0.1)	3.7 (0.0)
Attribution	4.4 (0.1)*	4.4 (0.0)
Physical contact	3.4 (0.1)*	3.5 (0.0)
FAD		
Overall Family functioning	3.3 (0.1)***	2.5 (0.0)

Regression analyses, corrected for age, GH trial, and GH dosage: * $p < 0.05$ *** $p < 0.001$; two-tailed (GH group vs. Population sample).

Table 5. Mean (SEM) of the 7 scale scores of the Utrecht Coping List

	GH group	Population sample
Active approach	2.3 (0.1)	2.4 (0.0)
Reassuring thoughts	2.5 (0.1)*	2.4 (0.0)
Expression of emotion	2.0 (0.1)	2.2 (0.0)
Palliative reaction	2.4 (0.1)	2.2 (0.0)
Passive reactional pattern	1.7 (0.1)	1.7 (0.0)
Seeking social support	2.6 (0.1)	2.3 (0.0)
Avoiding/Anticipating	2.1 (0.1)	2.1 (0.0)

Regression analyses, corrected for age, GH trial, and GH dosage: * $p < 0.05$; two-tailed (GH group vs. Population sample).

Child Depression Inventory (CDI)

Total depression scale scores were not significantly different to the Population sample scores (table 4).

Body Attitude Scale (BAS)

Attribution and Physical contact were scored slightly but significantly lower than the Population sample ($B = -0.26$, $p < 0.05$, $B = -0.41$, $p < 0.05$, respectively; table 4). Appraisal scores, however, were not significantly different to the Population sample scores.

Family Assessment Device (FAD)

The Total FAD scale scores were significantly higher than the Population sample scores ($B = 0.77$, $p < 0.0001$; table 4).

Coping (UCL)

Compared to the Population sample scores, only the scale Reassuring thoughts was significantly higher in the dose-response group ($B = 0.32$, $p < 0.05$). Scores for the scales Active approach, Expression of emotion, Palliative reaction, Passive reactional pattern, Seeking social support, and Avoiding/Anticipating were not significantly different to the Population sample (table 5).

Correlations between Tests

To assess possible relations between the results, which were significantly different from the Population sample, partial correlations were done, corrected for GH dosage. The Total HSP score was significantly correlated to the Total FAD score ($r = 0.38$, $p = 0.01$), the BAS Attribution score ($r = 0.61$, $p < 0.001$) and the BAS Physical contact score ($r = 0.57$, $p < 0.001$). No correlation was found be-

tween the Total HSP score and the UCL Reassuring thoughts score. Total FAD score was significantly correlated with the BAS Physical contact score ($r = 0.46$, $p = 0.001$), while no correlation was found between Total FAD score and the BAS Attribution score, or the UCL Reassuring thoughts score.

Effect of Final Height

FH SD score or corrected FH SD score, with or without correction for height SD score at start, showed no significant effect on Behavioral SD scores, Self-perception (Total HSP) scores, Depression scores, Bodily Attitude scores or Family functioning scale (FAD) scores. Correction for height SD score at start did not affect results.

Discussion

Our study presents psychosocial functioning results of women with TS after reaching FH in two GH trials. We measured psychosocial functioning by standardized questionnaires on behavioral problems, self-perception, depression, bodily attitude, family functioning, and coping. We show that after long-term GH treatment, behavior of the TS women was comparable to normal Dutch peers. In contrast, we show their self-perception, and their attitude towards their bodies was slightly less positive than for their normal Dutch peers. We found no evidence of increased symptoms of depression, TS women rated their family functioning higher, and had a slightly different coping pattern compared to their Dutch peers.

We show that self-rated problem behavior scores did not significantly differ from normal Dutch peers. Although we did not evaluate psychosocial functioning before start of GH treatment in our TS group, many studies have found that untreated adolescent girls with TS have more problem behavior than normal girls [24, 25]. Our results therefore suggest an improvement in problem behavior, after reaching a FH within the normal range for most and puberty induction at a pubertal age. According to Ross et al. [7] improvement in (parent-reported) behavioral problems could be explained by the estrogen substitution alone. In other studies, similar improvement in behavior can be found after several years of GH treatment [26, 27].

Regarding self-perception, our results show that after reaching a FH, in most cases, in the normal range while puberty was induced at a relatively normal age (12 years

in the majority), self-perception total score was significantly lower than in normal Dutch girls. We found that the TS women feel they are less socially accepted, are less athletic, and have a lower romantic appeal than normal girls. Similar findings have been reported in untreated girls and women with TS [28, 29]. Several studies, however, have shown that treatment with estrogens and/or GH treatment improved self-perception [7, 25, 26]. Whether, in our study, scores for self-perception were even lower before start of GH treatment, we cannot say. But, even if scores had improved during the GH trials, they did not normalize. A possible reason why self-perception remained lower than normal could be the insecurity brought about by having typical physical TS features. Another reason might be the incidental observation of both parents and clinicians that some girls seem to lack social graces. To substantiate this observation, a recent study showed TS women have an impairment in recognizing emotions on someone's face compared with normal women, possibly indicating anomalies in amygdala function [30]. Another reason why our TS group feels less athletic might be because they actually have a restriction in movement. Nijhuis-van der Sanden et al. [31] found that, although TS girls move with the same accuracy as their normal peers, they move with a significantly lower speed and conclude that TS girls have a problem in execution of movement. Due to the age of the participants (mean age of 18 years) the role of infertility was not investigated. Based on our professional experience, infertility has a larger role on self-perception later in life.

Several studies have found evidence of depression in TS women who were untreated or only treated with estrogens [32, 33]. In our group of TS women, after long-term GH treatment and estrogen substitution at a pubertal age, the results of the questionnaire show no significant signs of depression. A previous study on adolescent girls with TS treated with GH (100%) and estrogen (61%) described severe depressive symptoms in 20% [34] of the girls. The factor related to these symptoms was teasing by peers about their physical appearance. Rickert et al. [34], however, did not show any data on height gain or pubertal development during GH and estrogen treatment. Therefore, the discrepancy in results might be explained by differences in height gain or pubertal development. Since we found no evidence of depression, this might indicate the girls suffered less from teasing as a result of adequate GH and estrogen treatment.

Furthermore, our results show that after GH treatment and puberty induction TS women appraise their bodies

similarly to their peers. Other studies have shown that TS girls and women when untreated score their physical appearance significantly lower than their peers [28, 35]. Interestingly, the TS women have a small but significant tendency to attribute problems to their appearance and avoid physical contact. Although our group was adequately treated with GH and estrogen, we did not treat the typical physical TS features, other than short stature and absent pubertal development. It is therefore not surprising that they still feel insecure about their appearance.

Previous studies found girls with TS are often overprotected by their parents [26]. Overprotection, however, is also seen in other patient groups with short stature [36]. One of the reasons for parents to overprotect is lack of peer relations of their children. On the other hand, children with poor peer relations rely more on family functioning [37]. Several studies describe an increase in family functioning, parallel to an increase in self-concept and a decrease in behavioral problems during GH treatment [25, 26]. In our study, after reaching a FH within the normal range in most cases and puberty induction at a relatively normal age, we found that TS women have a better family functioning than peers. This might indicate that these TS women still lack peer relations and take refuge in their family as a way of coping with problems [25]. Another explanation might be that as a result of past medical and psychosocial problems these TS women and their families have faced, their families actually function better than peer families. Rovet et al. [26], in their controlled GH trial, found an increase in family functioning and explained this as a greater involvement of the parents due to the GH treatment.

Commonly, girls and women with TS are described as withdrawing from social interaction as a way of coping with problems [25, 38]. Interestingly, we show that women with TS, after long-term GH and estrogen treatment, have only a slightly different coping strategy than their peers. They used more Reassuring thoughts to cope with problems, while they used strategies such as Avoiding problems but also Active approach and Expression of emotions as often as their peers. These results seem to indicate that, in general, TS women, after adequate GH and estrogen treatment, have a 'normal' coping strategy.

When we looked at the relation between our results, we found that TS women, who have a good self-perception, also have a good family functioning, attribute problems less to their appearance and enjoy physical contact. These results strengthen the common suggestion that these TS women rely on family functioning more than other women [37], which for them leads to a

more favorable self-perception and bodily attitude. Previous studies have described that the TS women rely on their families more than other women as a way to avoid problematic situations [25, 37]. In the GH group, we show that these women avoid problems similarly to their peers.

As mentioned before, several studies show more behavioral problems in untreated TS girls and a decrease in problems during GH treatment [25, 26]. Similarly, for self-perception, an improvement has been found during GH and estrogen treatment [25, 26]. Although it is therefore likely that in our study, GH and estrogen treatment has had a positive effect on psychosocial development, we did not find significant relationships between test scores and (corrected) FH or a GH dosage effect. This might also indicate that GH treatment did not influence psychosocial functioning. Another explanation for this might be that the GH treatment regimen in the trials, regardless of the dosage, achieved its optimal effect on psychosocial functioning. Similarly, in short children born small for gestational age, while longitudinal results show a significant increase in psychosocial functioning during GH treatment, results did not differ between GH dosage groups [39]. In the present study, however, we are unable to show the extent of the effect of GH treatment, as we have no psychosocial data of start of the GH trials.

In conclusion, after long-term GH treatment, behavior of the TS women was comparable to normal Dutch peers. Although their perception of themselves and their attitude towards their own bodies was slightly less positive than for their normal Dutch peers, we found no evidence of depression. In addition, TS women rated their family functioning higher, and had a coping pattern very similar to their Dutch peers. TS women with a more positive self-perception also had a better attitude towards their bodies and had a better functioning family. These results show that even after reaching a height within the normal range and puberty induction at a pubertal age, some women with TS still experience psychosocial problems. It is, however, likely that GH and estrogen treatment improved psychosocial functioning. Long-term follow-up of these GH-treated patients will allow an evaluation of their life achievements.

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References

- Sas TC, de Muinck Keizer-Schrama SM, Stijnen T, van Teunenbroek A, Hokken-Koelega AC, Waelkens JJ, Massa GG, Vulsma T, Gerver WJ, Reeser HM, Delemarre-van de Waal HE, Jansen M, Drop SL: Final height in girls with Turner's syndrome treated with once or twice daily growth hormone injections. *Dutch Advisory Group on Growth Hormone. Arch Dis Child* 1999;80:36-41.
- Cacciari E, Mazzanti L: Final height of patients with Turner's syndrome treated with growth hormone (GH): Indications for GH therapy alone at high doses and late estrogen therapy. Italian Study Group for Turner Syndrome. *J Clin Endocrinol Metab* 1999;84:4510-4515.
- Johnston DI, Betts P, Dunger D, Barnes N, Swift PG, Buckler JM, Butler GE: A multicentre trial of recombinant growth hormone and low dose oestrogen in Turner syndrome: Near final height analysis. *Arch Dis Child* 2001;84:76-81.
- Quigley CA, Crowe BJ, Anglin DG, Chipman JJ: Growth hormone and low dose estrogen in Turner syndrome: Results of a United States multi-center trial to near-final height. *J Clin Endocrinol Metab* 2002;87:2033-2041.
- Van Pareren YK, de Muinck Keizer-Schrama SM, Stijnen T, Sas TC, Jansen M, Otten BJ, Hoorweg-Nijman JJ, Vulsma T, Stokvis-Brantsma WH, Rouwe CW, Reeser HM, Gerver WJ, Gosen JJ, Rongen-Westerlaken C, Drop SL: Final height in girls with Turner syndrome after long-term growth hormone treatment in three dosages and low dose estrogens. *J Clin Endocrinol Metab* 2003;88:1119-1125.
- Rovet JF: Behavioural manifestations of Turner syndrome in children: A unique phenotype? Turner syndrome in a life-span perspective: Research and clinical aspects. 4th International Symposium on Turner Syndrome, Gothenburg, Sweden, May 18-21, 1995. Amsterdam, Elsevier Science, 1995.
- Ross JL, McCauley E, Roeltgen D, Long L, Kushner H, Feuillan P, Cutler GB Jr: Self-concept and behavior in adolescent girls with Turner syndrome: Potential estrogen effects. *J Clin Endocrinol Metab* 1996;81:926-931.
- Simis KJ, Verhulst FC, Koot HM: Body image, psychosocial functioning, and personality: How different are adolescents and young adults applying for plastic surgery? *J Child Psychol Psychiatry* 2001;42:669-678.
- Standard Occupational Classification 1992. The Hague, Central Bureau for Statistics, 1993, p 185.
- Ferdinand RF, Verhulst FC, Wiznitzer M: Continuity and change of self-reported problem behaviors from adolescence into young adulthood. *J Am Acad Child Adolesc Psychiatry* 1995;34:680-690.
- Verhulst F, van der Ende J, Koot H: Manual for the Youth Self-Report (YSR). Rotterdam, Child and Adolescent Psychiatry, Sophia Children's Hospital/ University Hospital Rotterdam/ Erasmus University Rotterdam, 1997, p 233.
- Achenbach TM: Manual for the CBCL/4-18 and 1991 Profile. Burlington, University of Vermont, Department of Psychiatry, 1991.
- Achenbach TM: Manual for the Youth Self-Report and 1991 Profile. Burlington, University of Vermont, Department of Psychiatry, 1991.
- Achenbach T: Manual for the Young Adult Self-Report and Young Adult Behavior Checklist. Burlington, University of Vermont, Department of Psychiatry, 1997.
- Harter S: Manual of the Self-Perception Profile for Children. Denver, University of Denver, 1985.
- Harter S: Manual of the Self-Perception Profile for Adolescents. Denver, University of Denver, 1986.
- Kovacs M: Children's Depression Inventory. New York, Multi-Health Systems, Inc, 1992.
- Baardman I: Ingebeelde Ielijkheid. Amsterdam, Department of Psychology and Pedagogy, Free University, 1989.
- Byles J, Byrne C, Boyle MH, Offord DR: Ontario Child Health Study: Reliability and Validity of the General Functioning Subscale of the McMaster Family Assessment Device. *Fam Proc* 1988;27:97-104.
- Wenniger FM: Cross-national validity of dimensions of the family functioning: First experiences with the Dutch version of the McMaster Family Assessment Device (FAD). 1993; 14:769-781.
- Schreurs PJG, van de Willige G, Tellegen B, Graus GMH: De Utrechtse Coping Lijst: UCL, Omgaan met problemen en gebeurtenissen, Herzien handleiding 1993. Lisse, Swets & Zetinger, 1993, p 49.
- Bijstra JO, Jackson S, Bosma HA: De Utrechtse Coping Lijst voor Adolescenten. *Kind Adolesc* 1994;15:98-109.
- Schaufeli W, Dierendonck D: De betrouwbaarheid en validiteit van de Utrechtse Coping Lijst, een longitudinaal onderzoek bij schoolverlaters. *Gedrag Gezond* 1992;20:38-45.
- McCauley E, Ito J, Kay T: Psychosocial functioning in girls with Turner's syndrome and short stature: Social skills, behavior problems, and self-concept. *J Am Acad Child Psychiatry* 1986;25:105-112.
- Lagrou K, Xhrouet-Heinrichs D, Heinrichs C, Craen M, Chanoine JP, Malvaux P, Bourguignon JP: Age-related perception of stature, acceptance of therapy, and psychosocial functioning in human growth hormone-treated girls with Turner's syndrome. *J Clin Endocrinol Metab* 1998;83:1494-1501.
- Rovet J, Holland J: Psychological aspects of the Canadian randomized controlled trial of human growth hormone and low-dose ethinyl oestradiol in children with Turner syndrome. The Canadian Growth Hormone Advisory Group. *Horm Res* 1993;39:60-64.
- Siegel PT, Clopper R, Stabler B: The psychological consequences of Turner syndrome and review of the National Cooperative Growth Study psychological substudy. *Pediatrics* 1998; 102:488-491.
- McCauley E, Ross JL, Kushner H, Cutler GB Jr: Self-esteem and behavior in girls with Turner syndrome. *J Dev Behav Pediatr* 1995;16:82-88.
- Boman UW, Bryman I, Halling K, Moller A: Women with Turner syndrome: Psychological well-being, self-rated health and social life. *J Psychosom Obstet Gynaecol* 2001;22:113-122.
- Lawrence K, Kuntsi J, Coleman M, Campbell R, Skuse D: Face and emotion recognition deficits in Turner syndrome: A possible role for X-linked genes in amygdala development. *Neuropsychology* 2003;17:39-49.
- Nijhuis-van der Sanden MW, Smits-Engelsman BC, Eling PA, Nijhuis BJ, Van Galen GP: Low elementary movement speed is associated with poor motor skill in Turner's syndrome. *Dev Neuropsychol* 2002;22:643-670.
- Downey J, Ehrhardt AA, Gruen R, Bell JJ, Morishima A: Psychopathology and social functioning in women with Turner syndrome. *J Nerv Ment Dis* 1989;177:191-201.
- Deloos J, Van den Berghe H, Swillen A, Kleczkowska A, Fryns JP: Turner syndrome patients as adults: A study of their cognitive profile, psychosocial functioning and psychopathological findings. *Genet Couns* 1993;4: 169-179.
- Rickert VI, Hassed SJ, Hendon AE, Cunniff C: The effects of peer ridicule on depression and self-image among adolescent females with Turner syndrome. *J Adolesc Health* 1996;19: 34-38.
- Pavlidis K, McCauley E, Sybert VP: Psychosocial and sexual functioning in women with Turner syndrome. *Clin Genet* 1995;47:85-89.
- Sartorio A, Conti A, Molinari E, Riva G, Morabito F, Faglia G: Growth, growth hormone and cognitive functions. *Horm Res* 1996;45:23-29.
- Wide Boman U, Moller A, Albertsson-Wikland K: Psychological aspects of Turner syndrome. *J Psychosom Obstet Gynaecol* 1998; 19:1-18.
- Downey J, Ehrhardt AA, Gruen R, Morishima A, Bell J: Turner syndrome versus constitutional short stature: Psychopathology and reactions to height; in Stabler B, Underwood LE (eds): *Slow Grows the Child: Psychological Aspects of Growth Delay*. Mahwah/NJ, Lawrence Erlbaum Assoc, Inc, 1986, pp 123-138.
- Van Pareren Y, Duivenvoorden H, Slijper F, Koot H, Hokken-Koelega A: Intelligence and psychosocial functioning during long-term GH therapy in children born small for gestational age. *J Clin Endocrinol Metab* 2004;89:5295-5302.